VI. CONCLUSIONS.

1. Strychnine does not seem to affect the pulse when given simultaneously with alcohol.

2. In some cases (Experiments 1 and 3) strychnine seems to counteract in part the depressing effect of acute alcoholic poisoning on the respiration, and thus prolong life. The apparent exception (Experiment 2) is doubtless explained by the poor physical condition of the cat receiving strychnine and by the small dose.

3. Strychnine does not seem to interfere materially with the narcosis from acute poisoning with alcohol, but, apparently, does delay the onset of paralytic symptoms.

4. In subacute alcoholic poisoning (Experiment 4) strychnine seems to lessen the narcosis and paresis in the earliest stages, but in the later stages to increase the depression. However, a general conclusion is hardly justified, since only one control experiment was made.

5. Although in no case was the strychnine competent to completely remove the effects of the large doses of alcohol which were employed, yet it may be considered probable that appropriate doses of strychnine (fairly strong therapeutic doses) would prove useful in the treatment of poisoning from even lethal doses of alcohol.

6. No action on the nerve cells by either alcohol or strychnine was demonstrable histologically.

7. Many drugs depress the activity of yeast cells, but no reliable stimulant was found; therefore the antagonism of drugs in their action on these cells could not be studied.

8. Heat was found to be a reliable stimulant up to 45° C., but strychnine as an antidote to heat did not give uniform results at the successive temperatures, so that the antagonism is not a simple one.

BLOOD CHANGES IN DEMENTIA PARALYTICA.

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THE blood of patients suffering from dementia paralytica has been the subject of microscopic study by many observers during the past fifty years, but none have made regular and systematic examinations extending over a considerable portion of the course of the disease. Believing that such a study, so conducted as to eliminate all known physiological changes, might throw further light upon the nature of this important disease, this work was begun at the suggestion of Dr. August Hoch in the spring of 1901. The present is a preliminary report upon eleven cases.

HISTORICAL. The earliest known studies of the blood of paretics were made by Erlenmeyer and Hittorf in 1846 and 1847; Michale, 1848; Sutherland, 1873, and Voisin, 1879; but as their studies were made with instruments which would not give results comparable with our own, they are not taken into consideration.

Macphail,[1] in his study of fifteen cases of paresis, in which he laid special stress upon the blood state in different stages of the disease, ascertained that the hæmoglobin and erythrocytes were relatively low in the first stage, increased slightly during the quiescent period, and diminished greatly during the final stage, but showing, as a whole, a qualitative and quantitative diminution which runs parallel to the progress of the disease; also, that the leukocytes increased proportionately toward the end of the disease, and, finally, that states of excitement seemed to have an especially great influence upon the condition of the blood.

Thompson, as quoted by Macphail, in the examination of five typical cases of paresis in the stage of onset, the demented and the paralytic stages, found that within the first six months the hæmoglobin averaged 66.2 per cent., and the proportion of the white and red cells to be 1 : 308; six to fifteen months, hæmoglobin, 70 per cent., and whites and reds 1 : 176; and toward the end of the disease hæmoglobin 60.6 per cent., and proportion of whites and reds to 1 : 124.

The conclusions of Lewis, cited by Capps, were similar to those of Thompson.

Smyth,[2] in the study of forty cases of paresis in which the duration of the disease varied from the second to the thirty-third month, discovered that there was a diminution of hæmoglobin, except during periods of great exaltation, and a marked falling off in the number of red cells.

Winkler,[3] in four cases of paresis, three of whom were moderately nourished and one well nourished, found the hæmoglobin diminished as well as the number of red blood corpuscles. In one case they were high. They always diminished as the disease approached its termination. The changes of the blood were parallel with the loss of weight. In the stages of excitement the hæmoglobin and red blood corpuscles, both diminished at the onset, remained stationary in the period of quiescence and fell rapidly in the last stage. The body-weight presented a similar change, *i. e.*, in the stage of quiescence it remained the same or increased slightly, and in the end stages fell rapidly.

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[1] Journal of Mental Science, 1884, p. 378.

[2] Ibid., 1890, p. 504.

[3] Ueber Blutuntersuchungen bei Geisteskranken, Inaug. Dissert., Bonn, 1891, pp. 5-39.

Paralytic attacks had a bad effect upon the blood and produced a loss of weight.

Kryspiakiewicz[1] examined fifteen cases of paresis, mostly progressive cases and some during the terminal state and when suffering from acute decubitus. While his observations in general agree with those of Smyth, he also frequently found poikilocytosis, and a larger number of megalocytes and a smaller number of microcytes than is normally present.

Roncoroni,[2] in his study of fifteen paretics, in which he paid special attention to the eosinophiles, found that they were sometimes increased, sometimes diminished, but rarely normal, and that in paretic excitement there was regularly an increase, which in one case reached 25 per cent.

Burton, as cited by Somers, found in four cases of paresis a diminution of the leucocytes and of the hæmoglobin.

Somers,[3] in the examination of five cases of paresis, discovered a falling off of the erythrocytes and a slight increase of the leucocytes (8800), and a decline of the hæmoglobin (74.2).

Capps[4] in nineteen paretics found a more or less striking diminution of hæmoglobin (70 to 90 per cent.), but a steady increase was noted, dating from the admission to the hospital, which, by the author, was believed to be due to the improved hygiene and nutrition. In only four cases did the erythrocytes reach 5,000,000. There was present in the majority of cases a moderate leukocytosis, yet no conclusion could be drawn as to the relationship between the different stages of the disease and the degree of leukocytosis. He, however, failed to find a leukocytosis in two cases examined within four months of the onset, while one case of the same duration, but of rapid progress, did exhibit leukocytosis. In studying the variety of leukocytes, he found that the small lymphocytes were less numerous than normally, and the large lymphocytes were slightly increased, but sometimes three times the normal amount. The polymorphonuclear variety was slightly increased in fourteen of the nineteen cases, but in only one instance above 78.8 per cent.

Of rather more importance was his observations in reference to the blood changes at the time of a paralytic attack. Shortly preceding paralytic attacks, there was an increase of the erythrocytes and hæmoglobin, and shortly following them a very transitory but pronounced leukocytosis. The erythrocytes and hæmoglobin fell a few hours later. The intensity of the leukocytosis depended upon the severity and the duration of the attack.

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[1] Wien. med. Wochenschrift, 1892, No. 25.

[2] Archiv di Prichiat. Scienze, 1894, vol. xv., fasc. 111, p. 293.

[3] New York State Hospital Bulletins, January, 1896.

[4] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1897.

Jeliffe,[1] in his observations, which consisted of one examination in each of seventeen cases, ascertained that the hæmoglobin was reduced in nearly all cases, that the erythrocytes were comparatively high, the number being increased in fourteen of the seventeen cases, and in eight of these amounting to more than 6,000,000. The leukocytes were reduced in seven cases, and in only three cases was a leukocytosis recorded, and accompanied in each case a " general exalted condition." His observations on the differential count, in general, accords with those of Capps, except that the author calls attention to the complete absence of eosinophiles in some cases.

CASE I.—The patient developed his psychosis at the age of forty years. He was known to have been intemperate. The character of the disease, during the first twelve months, was one of simple progressive dementia, which did not necessitate confinement. He then, rather suddenly, exhibited great motor restlessness with violence, expressed many expansive delusions of a religious nature and some hallucinations, and consciousness became greatly clouded. He was admitted to the hospital two weeks later. The condition of paretic excitement continued without abatement for about one month, when it gradually disappeared, leaving the patient in a condition of profound dementia, with greatly impaired memory, clouded consciousness, paralysis of thought and volition, and emotional indifference. Extremely expansive and Nihilistic delusions were alternately expressed, while his conduct was characterized by occasional outbreaks of irritability and violence, but otherwise he was orderly. Physically, he presented fine muscular tremor, considerable inco-ordination, faulty articulation, exaggerated deep reflexes, and unequal pupils, which responded to light within narrow limits.

The patient was in this condition at the time the blood examinations were begun, and continued without appreciable change until the twenty-fourth month, when he gradually became noisy and extremely filthy, but did not show any other evidence of increased psychomotor activity. Meanwhile, he had improved greatly in nutrition. In the twenty-sixth month, following a rather rapid fall in nutrition, he suddenly developed an apoplectic attack, with left hemiplegia, from which he recovered in five days. He then, for the first time, expressed delusions of poisoning, and persistently refused food, with consequent rapid emaciation, and death twenty-two days later, preceded by somnolence and, finally, stupor. The paralytic attack was followed in twenty-four hours by a high temperature (104° F.) which subsided on the third day, but from that time until death there was a pretty constant daily variation of temperature, extending from 96.6° F. to 100° F. There was no evidence of an acute inflammatory process which might account for a leukocytosis. The weight fell rapidly during the final fourteen weeks, dropping from 157 to 85 pounds.

A post-mortem examination was not made.

The study of the blood in this case, which comprised sixty-one weekly examinations, began just after the subsidence of the paretic excitement. During the first month both the hæmoglobin, the erythrocytes, and leukocytes averaged below normal, but following this and during the entire quiescent period, except for four weeks preceding the paralytic attack, and when the nutrition was beginning to fall, the hæmoglobin averaged 85 per cent., thence the hæmoglobin fell to an average of 74 per cent., until it began to rise nine days before death, and two days before death reached 92 per cent.

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[1] New York State Hospital Bulletins, July, 1897.

The erythrocytes rose to normal and remained within normal limits until the fall in nutrition, when they fell to below normal, and remained there until the nine days previous to the paralytic attack, when they rose to normal and gradually increased until they reached 6,386,000 two days before death.

The leukocytes following the first four weeks remained high normal for two and one-half months, when they fell to low normal and at times below 5000, where they remained for ten weeks; then high normal for four weeks, followed for sixteen weeks by a count varying between 8600 and 6000, with one exception, when for a week they rose to 9500. Then, one week previous to the fall of nutrition, when both the percentage of hæmoglobin and number of erythrocytes diminished, the leukocytes fell to 5000 and remained subnormal, with one exception (6800), until the terminal rise which began sixteen days before the paralytic attack, but did not become a distinct leukocytosis until the ninth day following it. The leukocytosis reached its height seven days previous to death, and fell on the last count to 13,5000. Among the leukocytes the polymorphonuclear variety predominated throughout, the percentage of which varied from 5 to 26 per cent. above the normal; upon only one occasion did it approach normal, and then it was 71.8 per cent. The greatest increase appeared during the final leukocytosis, when the percentage remained above 92 per cent. during the last four counts.

Case II.—This patient gave the first evidence of his disease at the age of forty-two years. It was of gradual onset, with a loss of interest in his work and a lack of endurance. At times he was also forgetful. He, however, continued at work for seven months, at which time he rather suddenly developed many changeable delusions of grandeur, with a feeling of well-being and an increased activity. One month later, when admitted to the hospital, he showed a defect of memory for both recent and remote events, a pronounced feeling of well-being, some pressure of activity, together with the most extremely expansive delusions, insomnia, anorexia, and loss of weight. Physically, there were contracted pupils which were irresponsive to light, general muscular tremor, faulty articulation, some ataxia of the lower extremities, absence of knee-jerks, and a lack of muscular tone. In the ninth month he developed a condition of paretic excitement during which the first examination of the blood was made. After a duration of two months this condition suddenly disappeared, leaving the patient in a condition of deeper dementia. He continued mildly elated but orderly in conduct. After an intermission of five weeks the condition of great excitement returned and continued for one month, when it again vanished. He lost sixteen pounds in weight, and at the end showed great muscular weakness. At this time the feeling of well-being was replaced by one of despondency and fear of death, and all delusions vanished. While he was quite orderly in conduct, took some interest in his surroundings, aided in ward duties, and spent much time in reading, he had lost all power of endurance, and usually became so fatigued by afternoon that it was necessary for him to go to bed; at the same time speech became confused. The condition of muscular paresis gradually progressed, and terminated fatally in an attack of syncope four months later, the total duration of the disease being nineteen months.

The temperature during the last four months occasionally dropped to 96° F., and even 95° F., and rose to 100° F., and on a few occasions to 102° F. and 103° F. without any apparent cause. During the two weeks preceding the paralytic attack it was mostly subnormal. Ten days before death it rose to 100.6° F.; thence there was a daily rise and fall, varying between 100.8° F. and 97° F., reaching 101.8° F. on the day of death. There were no objective signs of an acute inflammation process. The weight fell gradually from the eleventh month, when it was 139 pounds, to 79 pounds at the time of death. An autopsy was refused in this case.

The blood analysis began during the height of his first paretic excitement. The first two examinations, which were made at an interval of twenty six days, showed the hæmoglobin to have risen from 73 to 100 per cent., and the leukocytes from 6500 to 10,300, while the erythrocytes remained at low normal. The remaining counts were made bi-weekly until the last two months, when they were made weekly. In the remission of five weeks the hæmoglobin remained between 77 and 83 per cent., the erythrocytes rose from low to high normal, while the leukocytes went up to 14,000 and then fell to 7800. In the period of excitement which followed this for two months, but which was not as intense, though it led to great physical weakness and the loss of nearly sixteen pounds in weight, the hæmoglobin varied between 76 and 102 per cent.; the erythrocytes remained normal and high normal, and rose at one time to 5,800,000, and there was a leukocytosis, except for one week, when the leukocytes fell to 8700. During the quiescent period of four months which followed the hæmoglobin varied from 62 to 89 per cent., but averaged 76 per cent.; the erythrocytes remained normal and high normal, except on two occasions, when they fell to 4,000,000, and 4,500,000; the leukocytes varied considerably, twice falling to nearly 6000 and once below, and three times showing a moderate leukocytosis; otherwise they were about normal. The examination of the blood on the day of the collapse showed the hæmoglobin at 67 per cent., the erythrocytes at 4,888,000, and the leukocytes at 8400. Six days later, while the patient continued to fail and at the time was in a semicomatose condition, the hæmoglobin rose to 82 per cent., the erythrocytes to 5,982,000, and the leukocytes to 16,000. Death occurred sixty hours later.

The differential count showed, throughout the whole psychosis, a great increase in the percentage of polymorphonuclear leukocytes, which reached at the last two counts 90 and 86.4 per cent.

Case III.—This case is not cited in full because of the limited study of the blood, which comprised two examinations, on the twelfth and seventh days before death.

The patient first gave evidence of the psychosis at fifty-four years of age. There was some insane collateral heredity, but otherwise no etiological factors could be ascertained. The disease was of gradual onset, and the symptoms were those characteristic of the demented form until one week previous to his commitment in the twelfth month, when he rapidly developed symptoms characteristic of the agitated form of the disease. This condition of intense excitement continued until he fell into a semicomatose state seven days before death, which gradually deepened, being accompanied by a dysenteric condition. The physical signs of the disease were well advanced at the time of his admission. The patient was much emaciated, which condition rapidly increased until death. There was no autopsy in this case.

In the two blood examinations the percentage of hæmoglobin was at first 90 per cent., but then fell to 65 per cent. The erythrocytes were normal, and then fell below normal; the leukocytes showed a leukocytosis (10,000), which advanced to 14,100, in which there was an increased percentage of polymorphonuclear leukocytes (84 and 86 per cent.).

Case IV.—The exact date of the onset of the psychosis and the character of its early symptoms are unknown. At the time of her admission she was thirty-four years of age, and the disease had already reached the stage of profound dementia, with complete clouding of consciousness, greatly impaired memory, emotional deterioration and a considerable emotional irritability, pronounced limitation in the store of ideas, considerable incoherence, some increased psychomotor activity, and complete inability to care for herself. Physically she presented Argyll-Robertson pupils; great ataxia, which necessitated confinement in bed; faulty speech, pronounced tremor of hand and of facial muscles, exaggeration of deep reflexes, and considerable emaciation. Two months previous to her commitment she had a series of epileptiform attacks.

At the time of the first blood examination, which was made thirteen days after admission, the patient was still showing some psychomotor activity, confined mostly to a purposeless fumbling with her clothing, sometimes tearing or removing it, and incessant talking in a loud voice, but this gradually disappeared by the end of the first month of her residence.

At this time there suddenly developed a paralysis of the left arm, unaccompanied by other phenomena. From this time the activity began to diminish. In the fourth month her mind had become a complete blank, acute decubitus appeared, and the terminal phalanges of the paralyzed left hand sloughed off. From this time paresis of all the muscles became more marked, acute decubitus advanced, and she died three months later, at no time showing a rise of temperature. The weight could not be taken in this case. Post-mortem examination corroborated the diagnosis.

The examinations of the blood were made bi-monthly in this case, and show, in reference to the percentage of hæmoglobin, that it averaged low, especially during the last month of the disease (68 per cent.). Previous to this it reached 90 per cent. only on two occasions. The estimation of the erythrocytes showed a normal and high normal count, except for the first and next to the last examinations, when it fell to 4,200,000. During the second and third months previous to death it varied between 5,150,000 and 5,666,000, but during the terminal month it fell below 5,000,000, was lowest thirteen days before death, and then rose to about 4,700,000 four hours previous to her death. The leukocytes remained below normal during the first three months, except on two occasions, when there was a very moderate leukocytosis

(9733 and 10,666). Thence for one and one-half months it was high normal, and thence for one week there appeared a leukocytosis of 14,000. It then dropped to normal and low normal, except on the twenty-seventh day before death and four hours before death, when it reached 10,100 in the former and 14,600 in the latter. In the differential count the polymorphonuclear leukocytes were constantly above normal, and in the final leukocytosis reached 94.2 per cent.

Case V.—This patient developed his psychosis at the age of thirty-five years. It was of gradual onset and characterized by a progressive deterioration in memory and judgment. Within a month he began to express numerous grandiose delusions, and showed considerable increase in activity. Two weeks previous to his admission to the hospital, in the twelfth month of the disease, he suffered from a series of epileptiform convulsions, followed by transitory paresis in the left arm and mentally by great clouding of consciousness and extreme activity, simulating the occupation delirium of senile dementia. This condition still persisted at the time of his admission. He was emaciated, insomnia was marked, the deep reflexes were abolished, the pupils did not react to light, and ataxia was marked. Dementia was profound.

At the time of the first blood examination, in the fourteenth month of the disease, the restlessness had somewhat subsided, but deterioration had advanced and emaciation had become still more prominent. He was, however, very loquacious. In the fifteenth month the activity began gradually to increase, and the patient became destructive, filthy, and very noisy. By the third week the excitement had become extreme, and continued so for one week, when the patient developed epileptiform attacks, which assumed the form of an epileptic status and lasted for twenty-four hours, followed by a semicomatose state, which terminated fatally eight days later. During his five months' residence in the hospital the patient gradually fell in weight from 123 pounds to about 85 pounds. The temperature was not taken during his final illness, but apparently was normal. An autopsy revealed the characteristic lesions of paresis.

In studying the condition of the blood, which was examined weekly until the final ten days, when four counts were made, we find that the hæmoglobin did not show any great variation. During the period in which the motor excitement had subsided, it rose to 90 per cent. on three occasions, but from that time on it remained pretty constantly about 85 per cent., with one exception, which was the day following the epileptic status, and then it fell to 76 per cent. The erythrocytes remained about normal until the final excitement, when they gradually rose until the day following the convulsions, then fell to normal, but four days later, which was three days previous to death, they had reached 6,333,000. The leukocytes remained below normal until the appearance of the great excitement preceding the convulsions, when a leukocytosis appeared. This reached 17,200 the day following the convulsion, but had dropped to 14,200 three days before death. We find among the different forms of leukocytes present that the polymorphonuclear variety was always above 79 per cent., and during the terminal leukocytosis reached 93.4 per cent.

Case VI.—The patient developed her psychosis at the age of forty-one years. The onset was gradual and characterized by despondency, delusions of self-accusation and fear, but further than this the nature of her psychosis was unknown until her admission to the hospital one year later. At this time she was profoundly despondent, showing great apprehension and expressing fear of death. She was greatly agitated and lamented loudly. In fact, the clinical picture was that of the so-called "agitated melancholia." Physically she presented marked emaciation, anorexia, and constipation, but none of the characteristic physical symptoms of dementia paralytica. In the fifteenth month of the disease she began to improve rapidly, and in the course of one and one-half months had apparently recovered, in this time having gained ten pounds in weight.

During the succeeding twenty-five months the patient seemed quite normal, except that she exhibited a greater tendency to indulge in alcoholic excesses.

The disease gradually reappeared at the age of forty-three years. She began to neglect her household duties and her own personal appearance, would serve her meals uncooked, stole money from her husband and spent it for liquor, attempted to travel away from home without money, and at times was threatening. Upon admission to the hospital three months from the onset it was found that she had already greatly deteriorated, especially in memory and judgment. Many absurd and extremely grandiose delusions were expressed. There was marked emotional deterioration, while her volitional condition exhibited stupor, relieved at times by some pressure of activity, volubility, and a feeling of well-being, with impulsive violence. Physically she presented an absence of tendon reflexes, pupils that were unequal and refused to react to light, faulty articulation, considerable muscular tremor, some ataxia, and general lack of muscular tone. In the fifth and sixth months dementia had gradually advanced, while the stupor and occasional excitement had disappeared. In the seventh month stupor, with negativism, appeared. She refused food, resisted everything, and displayed no voluntary activy. The stupor increased, the loss of weight and general paresis became marked, and death occurred in the sixth week of the stupor. The temperature was slightly subnormal during the last week, and at the time of the final blood examination on the day of the death was 93.4° F. in the axilla. A permission for a post-mortem examination could not be secured.

The blood examinations in this case were confined to the period of final stupor. The first examination was made in the second week of the stupor, at a time when the state had not become very profound, and the last about ten hours before death, the counts being made at weekly intervals.

In the five examinations there was a rapid diminution of the percentage of the hæmoglobin from 85 to 60 per cent. for the first four, and then a final rise to 65 per cent.; the same change occurred in the count of the erythrocytes, which dropped from 5,488,000 to 3,711,000 and in the final week rose to 4,484,000. On the other hand, the leukocytes were below normal for the first two weeks and then showed an increasing leukocytosis, which reached 25,000 the day of her death. Throughout the whole period the increase in the number of leukocytes was largely represented by an increase of the polymorphonuclear leukocytes, which never fell below 82 per cent.

CASE VII.—In this case the disease appeared gradually at fifty-four years of age. At first it was noticed that the patient began to drink to excess. He then became drowsy and heavy and slept a great deal of the time. Details of his work were overlooked, and he showed great irritability. Morally he lost his sense of propriety and was occasionally obscene. Under the influence of rest and total abstinence he gradually improved from the sixth to ninth month, and from the ninth to seventeenth months seemed " nearly well " and " perfectly natural."

In the seventeenth month, following exposure and overwork on the farm, he began to express delusions of grandeur and show some psychomotor restlessness, which with great irritability made his confinement in an institution necessary seven weeks later. At this time he presented some time disorientation; slight incoherence in his train of thought; impairment of memory and many changing delusions of grandeur of the most florid type, involving every sphere of life. There was also a pronounced feeling of well-being, with considerable emotional irritability and lack of moral feelings. His pressure of activity was confined mostly to an intense busyness, writing important letters, sending telegrams, etc. Physically there were exaggerated tendon reflexes, Argyll-Robertson pupils; muscular tremor, especially of facial muscles; incoordination and greatly impaired articulation.

This condition of excitement greatly increased, and at the time of his first blood examination, one month later, was extreme. His sleep was greatly disturbed and he had lost nineteen pounds in weight. The excitement began to abate in the second and third months, so that it was possible to keep him clothed. Suddenly the patient developed a stuporous condition over night. In the morning his consciousness was found to be greatly clouded, memory was much impaired, he was silent, and only fragments of his former grandiose ideas could be obtained by direct questions; emotionally the elation had been replaced by indifference, and his activity had mostly disappeared. Physically muscular exhaustion with increased tremor and inco-ordination had appeared, the countenance had become ashen and sunken. This stupor increased and death occurred thirty-six hours later, in the twenty-third month of the disease. During the week previous to the appearance of the stupor his weight fell eight pounds. The temperature was slightly subnormal during the stupor.

Consent for post-mortem examination could not be obtained, and the diagnosis could not be verified.

The examination of the blood, which consisted of bi-weekly examinations, shows the hæmoglobin to have remained subnormal until the day previous to the appearance of the stupor, when it rose to 105 per cent. The erythrocytes were subnormal at the time of the first examination, but had increased 1,000,000 by the second examination, then they steadily fell with the slight abatement of the excitement until the day before the stupor, when with the hæmoglobin they rose to 5,088,000. The leukocytes were subnormal until the last examination, when they rose over 3000, producing a slight leukocytosis. In this elevation the polymorphonuclear leukocytes jumped up about 20 per cent., with a corresponding drop in the small lymphocytes, which had been 37.2 per cent. and 39 per cent., but with this exception the character of the leukocytes had been normal.

This case is of greatest interest because it shows the tendency to an abrupt rise in all three elements of the blood one day preceding the appearance of the fatal stupor.

CASE VIII.—At forty-six years of age this patient began to "fail in health," to lose in weight, and suffer from malaise; but it was not until seven months later that mental symptoms appeared, at which time he neglected his work, became loquacious and displayed a moderate feeling of well-being. A few somatic delusions were expressed, such as that he had revolving wheels in his head, which he feared would wear through the cranium and cause death, and his memory for recent events was impaired. He was admitted to the hospital three months later, when he was partially disoriented, and showed marked impairment of memory, some feeling of well-being, and motor restlessness. Physically he presented ataxia, general muscular tremor, faulty speech, Argyll-Robertson pupils, exaggerated reflexes, and impaired nutrition. In the course of two months the restlessness and loquacity disappeared, consciousness cleared, somatic delusions vanished, and nutrition improved. Constant hallucinations of hearing, however, appeared, with delusions of infidelity and of reference, which made him despondent. It was at this time that the blood examinations were begun. He was orderly in conduct and an excellent helper in the ward.

His mental condition remained unchanged during the succeeding six months. The hallucinations of hearing continued and caused him much anxiety in reference to his wife. During the latter part of this period he suffered from insomnia and terrifying dreams and steadily lost in weight. The physical symptoms had not advanced. Without warning he suddenly became greatly agitated, reacted to numerous hallucinations of hearing, assaulted fellow-patients and attendants, resented his confinement, removed his clothing without purpose, and exhibited great motor restlessness. Consciousness remained clear. Food was refused and sleep completely abolished. At the end of the fourteenth day the patient became comatose and died forty-eight hours later.

During the quiescent period his weight gradually fell fourteen pounds, and during the final period of excitement dropped thirty-six pounds. The temperature was not taken, but from all external indications was normal.

A study of the tabulated record of the blood examinations shows that the erythrocytes throughout the period of quiescence, extending from the twelfth to the eighteenth month, with few exceptions, remained constantly normal and high normal. During the eight weeks previous to the terminal excitement there had been a gradual rise for seven weeks and then an abrupt drop of 900,000. In this same period the hæmoglobin at first averaged about 89 per cent., when it fell and averaged during the last thirteen weeks about 82 per cent. The leukocytes at first continued about normal, but during the last thirteen weeks of this period fell to low normal, and sometimes even to 5000. The week previous to the exacerbation a leukocytosis appeared. In the differential estimation of the leukocytes we find that the polymorphonuclear leukocytes were always in excess of the normal percentage by ten to fifteen points, while the small lymphocytes presented a continuous lymphocythæmia. The large lymphocytes were continually below normal during the latter part of this period.

The final period of the disease, that of the excitement, presents a marked change. In the first place, there was a progressive increase in the number of the erythrocytes after the second week, reaching, eight hours before death, 7,551,000; the hæmoglobin showed a corresponding rise to 110 per cent. The leukocytes from the week preceding the exacerbation began to increase, and in the final count reached 27,000. The increase occurred entirely in the polymorphonuclear variety, which at the end averaged 91.6 per cent.

The post-mortem observations in the case verified the diagnosis of general paresis, and failed to reveal any cause for the leukocytosis.

CASE IX.—The onset of the disease occurred at forty-three years, six months previous to the patient's admission to the hospital. He began to drink to greater excess, and when under its influence became violent. His work was abandoned while he spent his time loafing about the neighborhood. He presented a feeling of well-being, and in a short time expansive delusions appeared. He was shiftless and careless, and upon two occasions set the house on fire with ashes from his pipe, but on neither occasion made any effort to extinguish the flames. At the time of his admission he was still expansive and had a feeling of well-being. Deterioration was evident from his impaired memory and judgment and lack of emotional reaction. There was no increased activity, and consciousness was clear. Physically the pupils were unequal and irresponsive to light, tendon reflexes were absent, and there was faulty speech, general muscular tremor, moderate ataxia, and greatly disturbed speech. From the eighth to tenth months the expansiveness and feeling of well-being gradually disappeared, while the irritability increased, leading to occasional outbursts of passion with destructiveness. In the tenth month he suffered from his first epileptiform attack, preceded for a couple of days by lightning pains in his legs and followed by great restlessness and violent aggressiveness. During the following five months periods of composure with insight and fear of impending death alternated with periods of restlessness, irritability, and threatening and violent behavior. In the thirteenth month the second paralytic seizure occurred, preceded by five days of excitement and followed by composure. During the sixteenth to twenty-first months he had a partial remission, with an improvement in memory, emotional attitude, and conduct.

The first blood examination was made during this remission, but the second examination was not made until the termination of the remission, with a stupor in the twenty-first month. The examination was made on the second day of the stupor, when the patient was completely clouded, experiencing hallucinations of sight, incoherenec of thought, and slight restlessness. On the same day an epileptoid spasm of the clonic form appeared, involving only the right upper and lower limbs, followed by hemiparesis of this side lasting some days. The stupor disappeared in the course of five days, but mental deterioration had advanced, and the patient presented greater languor, indifference, and irritability. For the three succeeding months he showed considerable gradual improvement. Dazedness again suddenly appeared in the twenty-fourth month, with evident hemiparesis of the left side, from which he never fully recovered He remained semistuporous for two months, was thoroughly disoriented, and memory for all of the events of his life was greatly impaired. During this time he suffered from an epileptiform attack involving the left side and followed by a partial paralysis of this side. The convulsive twitchings lasted several days. The quiescent stage followed from the twenty-sixth to the twenty-ninth months. Another and exactly similar seizure to the above, involving the left side and producing paresis, occurred in the twenty-ninth month. The twitching continued for four days. Two weeks later a slight clonic seizure occurred involving the left side. Three days following this the patient developed a comatose state, with twitching of the right hand, weakened pulse, and febrile temperature, appearance of bronchopneumonia on the ninth day, and death on the eleventh day.

The post-mortem examination disclosed the anatomical lesions characteristic of dementia paralytica and also bronchopneumonia.

The study of the blood in this case began during the remission between the sixteenth and twenty-first months. At that time there was a moderate leukocytosis and a high erythrocyte count. The second examination was made on the second day of the stupor which followed the remission, and from this time examinations were made weekly until death. Six hours previous to the second examination the patient developed an epileptoid attack which lasted ten hours. Throughout this stupor the erythrocytes remained a high normal, with hæmoglobin varying between 85 and 95 per cent.; the leukocytes showed a leukocytosis 11,000 to 20,000, which reached its height in the second week. During the following ten weeks, while dementia was gradually progressing, the hæmoglobin remained high, for three weeks being above 100 per cent., but during the last two weeks falling below 75 per cent. The erythrocytes continued high, upon two occasions passing the 6,000,000 mark. The leukocytes fell abruptly to below normal, then rose slightly in the third, fourth, fifth, and sixth weeks, maintaining a slight leukocytosis, and again in the eighth week reached 10,300. In the tenth week, on the day when the condition of dazedness suddenly appeared accompanied by hemiparesis, the leukocytes reached only 9500.

From this time until three weeks previous to death, while the mental condition did not change greatly, the progress of the disease was marked, however, by paralytic attacks. The hæmoglobin averaged 80 per cent., upon one occasion reaching 65 per cent., the erythrocytes remained about 5,000,000 until during the final eleven weeks, when they averaged about 4,700,000, except upon one occasion, when they rose to 5,546,000, and fell back again the next week without apparent reason. During the final comatose state of two weeks the erythrocytes fell to 4,131,000, and on the day before death to 3,600,000.

The leukocytes during the period from the twenty-third to twenty-ninth month were mostly below normal, except near paralytic attacks. The week following the attack in the twenty-third month they reached about 10,500. They were then subnormal until the next attack, which lasted three days. The count was made on the day following the onset and showed a leukocytosis which continued into the next week. Four and five weeks later a leukocytosis appeared without any evident change of the mental symptoms. Likewise five weeks later and also seven and eight weeks later a slight rise above normal occurred. The next rise occurred thirteen hours preceding an attack, and again three weeks later a moderate leukocytosis accompanied another attack. In the coma which followed this attack and led to death the leukocytosis was 13,700, and one week later, the day previous to death, 10,700. In the differential count we find that during the periods of leukocytosis throughout the disease the polymorphonuclear leukocytes predominated in percentages varying from 60.6 to 90.4 per cent., but upon only two occasions being below 70 per cent. His weight charts show a gradual fall from the twenty-third month, and during the last two weeks a loss of over ten pounds.

His temperature at the time of the blood counts did not vary over a degree from normal, except during his final illness, when it remained subfebrile, except at the final count, when it was 105° F., ten hours after developing bronchopneumonia.

CASE X.—The onset of the psychosis was gradual at the age of thirty-five years, with a pronounced change of character, the patient becoming irritable, very forgetful, and at times dazed. Within a month of the onset he had a paralytic attack, and following this the memory was more impaired, and he seemed uneasy, and could not apply himself to his work. His memory and judgment had so far deteriorated by the tenth month that he was incapable of doing any work. At this time he began to express delusions of grandeur and to exhibit a feeling of well-being.

He was admitted to the institution in the twelfth month of the disease, with profound deterioration in both memory and judgment, clouded consciousness, extremely expansive delusions, and a marked feeling of well-being. He was busy in planning various grandiose business adventures, and had no thought or feeling for his family. Physically he presented an absence of knee-jerks, Argyll-Robertson pupils, inco-ordination of lower extremities, faulty articulation, general muscular tremor, absence of facial expression, and impaired nutrition.

During the first month after admission the patient showed some improvement, his consciousness became clear, the expansive delusions were less prominent. He became interested in his environment and was an excellent, energetic ward helper. Physically his state of nutrition improved greatly, and his weight rose seventeen pounds. There was no further change in his condition from the thirteenth to the twenty-third month. The blood examinations had been begun during the quiescent period.

In the twenty-third month the patient gradually developed a condition of stupor, he lost his former interest, stood about in one place unobservant, seemed unable to comprehend questions, and answered very slowly, giving evidence of difficulty of thought. All the delusions had disappeared and he expressed some insight into his condition. He was confined in bed. In seven days his stupor had deepened so that he did not respond at all to questions, and had to be fed by spoon. His weight continued to fall rapidly and his countenance became ashen. On the fourth day his temperature rose to 104° F., then fell to subnormal for two days, and from that time continued to show a slight afternoon rise to about 99.6° F. The stupor became more profound, and he died on the fourteenth day. In the two weeks his weight had fallen from 151 to 107 pounds.

In reviewing the blood charts of weekly counts which began during the quiescent stage at the seventeenth and one-half month of the disease we find that the hæmoglobin remained constantly low throughout this period. Upon three occasions it rose above 90 per cent., once to 93 per cent., and fell as low as 74 per cent.; its average, however, was 84 per cent. During the seventeenth and eighteenth months it varied between 87 and 93 per cent., while during the final two months it varied between 88 and 74 per cent. During the period of stupor it fell at first to 65 per cent., and then rose gradually to 90 per cent. at the final count—four days before death.

The erythrocytes during the period of quiescence remained mostly normal, three times they rose above 5,500,000, and once to 5,871,000, until they fell with the hæmoglobin, and from that time until the final stupor remained below 5,000,000, once reaching 4,500,000. During the stupor they gradually rose from 4,500,000 to 6,500,000.

The leukocytes, similarly with the erythrocytes, remained about normal, with one exception, when they rose to and over 10,000, then fell and were subnormal, averaging about 5,000. During the first part of the stupor, while it was still not profound, they rose gradually to normal, and then passed into a state of leukocytosis.

In reference to the relation maintained by the different forms of leukocytes we find that the polymorphonuclear leukocytes were about normal until the appearance of the leukocytosis, when they rose to 80.4 and 86.2 per cent.

During the final stupor there was a pronounced lymphopenia, while the large lymphocytes remained at the same percentage.

The autopsy in this case substantiated the diagnosis of dementia paralytica.

CASE XI.—This patient developed dementia paralytica at the age of thirty-six years, but did not come under our care until one and one-half years later.

At this time he presented as evidences of the disease an impairment of memory, some clouding of consciousness, emotional deterioration, and increased motor activity, and an extremely limited content of thought. Physically he presented a very pronounced choreiform condition, which simulated very closely advanced Huntington's chorea; also exaggerated deep reflexes; tremor of the muscles of the face, tongue, and hands, inco-ordination of the limbs and facial muscles, and a moderately defective speech. In reading there was an elision and an occasional translation of syllables. He was also poorly nourished.

The patient was in this same condition at the time the blood examinations were begun, which was in the twentieth month of the disease, one and one-half months after admission. His condition did not change until the latter part of the twenty-third month, when he would become dazed for a few hours at a time. While in this state he was completely clouded, and would fail to respond to the dinner call. In three weeks he gradually passed into a stuporous state. The duration of this stupor was from February 19th to April 14th, when he emerged from the condition during a night. The next morning he was active and interested, asked for work, and talked freely of his war experiences. There was no motor restlessness. His condition of deterioration had apparently not advanced during the stupor, while the choreiform condition had greatly improved and was now confined entirely to the muscles of the face.

A condition of stupor, similar in every respect to the former one, came over him suddenly on June 30th, ten weeks later. On the morning of the tenth day he seemed somewhat improved, as he voluntarily went to the bath-room; a few minutes later he fell in a convulsion and expired in three minutes.

The post-mortem examination in this case substantiated the diagnosis of dementia paralytica.

In this case the blood examinations were begun during a condition of moderate paretic excitement, which persisted until the gradual appearance of a stuporous state in the twenty-third month. During the first three months only four examinations were made. Following this for three months they were made weekly, and during the last two months bi-weekly. During the first three months the hæmoglobin varied between 70 and 95 per cent., the erythrocytes were normal, with one exception, when they fell to 4,511,000, and the leukocytes were low normal and subnormal. During the stupor of two months' duration the hæmoglobin varied from 65 to 85 per cent., the erythrocytes increased from subnormal to above normal, and then fell to normal; the leukocytes averaged low normal. In the period of two weeks' intermission the hæmoglobin varied from 68 to 80 per cent., the erythrocytes remained normal, and the leukocytes averaged normal. No blood count was made during the eleven days previous to the onset of the second stupor, and the final examination was made six days before death. This examination revealed a normal count, with the exception of the low hæmoglobin and the high percentage of the polymorphonuclear leukocytes (77.8 per cent.).

The clearly defined periods of stupor are not indicated by a definite blood change. The weight, on the other hand, shows a progressive drop from the time of the first examination to the time of death, a loss aggregating forty-four pounds.

TECHNIQUE. The blood has been drawn from the finger, preferably a middle finger, precautions being taken to avoid the application of friction and pressure. The hæmoglobin has been uniformly estimated with a Fleischl's hæmometer, attention being paid that all excess of blood is carefully wiped from the end of the capillary tube. The erythrocytes have been counted with a Thoma-Zeiss hæmocytometer, the same pipette being used for practically all of the work. In using Gower's solution, making a dilution of 1 : 200, an attempt has always been made to place the cover-slip over the Zappert counting chamber as rapidly as possible after placing the blood in the chamber. Two large squares in each of two drops and one in the third drop, preferably squares near the periphery, have been counted in making the estimation. Wherever there was great variation another drop has been counted, and the three counts nearest each other selected in making the aggregate.

In counting the leukocytes acetic acid solution, with a dilution of 1 : 20, has been uniformly employed. Three fields of four hundred squares each have been counted in each case, and if there was a great variation an additional field was counted.

As regards the personal equation, the greatest part of the work has been done by a single observer. The work was begun by Mr. Burr, laboratory technician, in the spring of 1901 (thirty counts), continued by Mr. Stone, medical interne (sixty counts), and completed by Mr.

Ward, technician, all of whom had had considerable experience in blood work. Besides this, parallel counts were made to determine the presence of any error due to personal equation.

In reference to the condition of the patient, every precaution was taken to have the work uniform. In most cases the examinations were made weekly, occasionally bi-weekly. They were made at the same time of day, either two hours after breakfast or an hour and one-half after a dinner, and on the same day of the week. All patients were on uniform diet.

In enumerating the different forms of leukocytes, five hundred cells were counted.

HÆMOGLOBIN. In interpreting the results of our observations the standards established by Reinert in his extended series of observations upon normal individuals have been followed. The results of Reinert have been confirmed in great part by Mr. Ward, who also made a series of twenty-four-hour counts upon normal individuals. In order to ascertain if daily pathological variations occurred in the paretic, a similar series of twenty-four-hour counts was made by him in one of the patients.

In all of the eleven cases the observations were necessarily confined to a period of the disease in which the disease process was already well established.

The hæmoglobin in all cases showed a moderate anæmia, which became more marked, but never profound (below 65 per cent.) as the disease advanced. In cases where the hæmoglobin was below 80 per cent. at the time of the first examination it did not subsequently vary much.

During the terminal state the average percentage of hæmoglobin in all but three of ten cases (IV., V., and X.) was from 3 to 20 per cent. higher than during the period just preceding. Of the three cases in which the rise in hæmoglobin was not coincident with the onset of the terminal state, there is in one a rise in the last four weeks from 65 to 70 per cent., in another during the last three weeks a rise from 65 to 90 per cent., and in the third case a rise in the last week (two counts) from 76 to 86 per cent. The only exception to the increase of the percentage of hæmoglobin in the terminal state is found in Case VI., in which the blood was examined only during this period. In this case there was a progressive drop in four weekly counts from 85 to 60 per cent.

In reference to the relationship between the condition of nutrition and the percentage of hæmoglobin, four of the eleven cases were well nourished throughout the period of examination until just preceding and during the terminal state, and seven were poorly nourished. The hæmoglobin in the well-nourished cases averaged only 4 per cent. higher than in the poorly nourished—78 and 82 per cent. In two of the well-nourished cases the hæmoglobin reached 100 per cent., and plus three times in one, and once in another case and three times in one of the poorly nourished patients.

The hæmoglobin during the various paretic states of quiescence, of excitement and stupor, not terminal, present no constant change, characteristic either of different states in the same individual or of similar states in different individuals. There was no increase in the percentage of hæmoglobin during the quiescent period, when nutrition regularly improved.

ERYTHROCYTES. The erythrocytes in eight cases in which the examinations extended over many months averaged normal in all, while in the two cases (III. and VI.) in which the examinations were made only during a short period previous to death the average was low normal, but in no case was there an average subnormal count. Occasionally the cells sank to low normal, but in only five instances did they fall to subnormal; in one case once, in one case twice, and in one case three times. In the last two of these cases it occurred at the very end of the disease.

In all cases the erythrocytes showed a tendency to sink during the period just previous to the terminal state, and then there occurred during the terminal state, with only one exception, a rise which is even more marked than that seen in the hæmoglobin during the same period. This rise varied from 5000 to 3,000,000, and in four cases became a polycythæmia. This rise was exactly coincident with the beginning of the terminal state in only five of the ten cases.

The various paretic states, exclusive of the terminal state, namely, those of excitement, of stupor and quiescence, failed to exhibit any change in the erythrocytes. In the five cases of paretic excitement the count averaged normal in all but one, which was subnormal. In the two cases with the greatest excitement, in one of which there were two periods of excitement, the count averaged normal in one case and in one period of the other, and low normal in the other period. In the individual cases the count during the period of excitement averaged the same in two cases and lower in one. In one of the two cases in which it was higher the excitement occurred early in the disease, when the erythrocytes are naturally higher.

Stupor occurred twice in each of two cases. In three of these four stuporous states the count averaged normal, and in the other subnormal. In the individual cases the erythrocytes averaged higher during the period of stupor in one case and lower in the other.

Periods of quiescence could be studied in eight cases, in one of which it occurred twice. In five of these periods the count averaged normal, in two low normal, in one high normal, and in one polycythæmia. In the individual cases the erythrocytes during the period of quiescence averaged about the same as during the other periods of the disease in three cases, lower in one case, and higher in the fifth case. In the remaining three cases there were no other paretic states except the terminal with which to compare it.

As regards the relationship between the condition of nutrition and the number of erythrocytes, the gradual, though not marked diminution in the number of cells as the disease advanced corresponded with the gradual loss of weight, except in the terminal state, when there was a tremendous loss of weight, but a considerable increase in the number of cells. In the three well-nourished cases (I., VIII., and X.) the erythrocytes averaged only a very little higher than in the poorly nourished cases.

In making the differential counts no qualitative changes of any moment were noted in any of the cases. Occasionally poikilocytosis, and now and then a single normoblast or a myelocyte, was found.

Paralytic attacks occurred in three cases. No appreciable change was observed in the erythrocytes near these times. In Case IX. the count was made at the time of the first attack, about six hours after the seizure; at the second, eighteen hours before; at the third, twenty hours afterward, and at the fourth, three days later. In Case I. the examination was not made until forty-eight hours after the attack. In Case V. the count was made a few hours after the termination of an epileptiform status of twenty-four hours' duration.

LEUKOCYTES. The study of the leukocytes does not show uniform results. In the cases in which the study extended over many months, the leukocytes presented a gradual fall in three cases, in three cases they were low at the time of the first examination and continued low, while in three cases they varied throughout the entire period. But in all of these nine cases just preceding, coincident with or following the onset of the terminal state, there appears a rise in the number of the leukocytes, which in all but two reaches a leukocytosis. This leukocytosis varies from 10,700 to 27,000. In the two cases which did not reach a leukocytosis there is a rise in one of 1000 and in the other of 3000. In three cases the height of this leukocytosis occurs before the final examination; in Case IX. there is a fall of 3000 in the last four days; Case V., a fall of almost 3000 in the last four days; and in Case I., a fall of 10,400 in the last five days. In the two cases in which the examinations are confined to the terminal state, there is in one a gradual rise from 6300 to 25,000, and in the other a leukocytosis which rose from 10,000 to 14,000.

The paretic states of excitement, of stupor and quiescence, exclusive of the terminal states, did not present any characteristic change. In the four periods of stupor—two cases— there was a constant leukocytosis in one, an average normal count in two, and a low normal in one, but in two of these periods a leukocytosis appeared transitorily. In six periods of excitement—five cases—there was an average hypoleukocytosis in three, an average normal count in two, and a leukocytosis in one. Besides this a leukocytosis appeared transitorily in one period of excitement. In the nine periods of quiescence—eight cases—an average normal count was present in four, a leukocytosis in one, a hypoleukocytosis in two, low normal in one, and a high normal in one, but in seven of these periods a moderate leukocytosis appeared temporarily.

The percentage of the different forms of leukocytes, shown by the differential counts, presents a striking abnormality. A uniform pathological increase of the polymorphonuclear variety occurred in ten of the eleven cases. In this one, Case VIII., the percentage of polymorphonuclear leukocytes remained within normal limits with two exceptions; once it fell to 53.8 per cent., and once it rose to 71.8 per cent. This pathological increase became more pronounced and reached its climax, with one exception, during the terminal stage. In Case II. the highest point is touched during a stage of excitement some months previous to the terminal state, but the average highest percentage occurred during the terminal state.

Plasma cells were carefully looked for in the differential counts, but never encountered. This observation is of importance because of the prominent rôle played by these cells in the vascular changes in the brain, which has come to be regarded as a pathognomonic condition.

The opportunity for observing the condition of the leukocytes near paralytic attacks was limited, as in the eleven cases only six attacks occurred—four in Case IX. and one each in Cases I. and V. In Case I., in which the count, made two days after the attack, was 8300, it is practically of no value. In Case V. the count, made a few hours after the termination of an epileptiform status of twenty-four hours' duration, was 17,200. This was in the terminal state, and five days later, three days before death, the count had dropped 3000. In Case IX. a count was made six hours after the first attack and showed a leukocytosis of 14,000. One week later the count was 19,000 without any apparent reason, except that the patient was still in stupor. The count was made in the second attack twenty-four hours later and showed a leukocytosis of 13,900, which was a rise of over 7000 above the average of the preceding weeks. Two days later the count was 14,600. In the third attack the count made eighteen hours before was 10,300, while for the two previous examinations it was under 7000, and the two subsequent examinations under 8500. In the count made three days following the fourth attack, which was during the terminal state, the leukocytosis reached only 10,000, which was a rise of 2000 over the previous count.

In reviewing the blood changes observed in the hæmoglobin and erythrocytes, there are only two conditions requiring special comment: the progressive moderate anæmia, and the tendency to a polycythæmia and an increase in the percentage of the hæmoglobin in the terminal state. The anæmia, which is more apparent in the hæmoglobin than in the red cells, is similar to that which accompanies chronic diseases; as, chronic nephritis, cirrhosis of the liver, and syphilis, except that it is less pronounced. It is in accord with the progressive atrophy of the nervous system accompanied by a gradual and complete loss of function, as well as atrophy and arteriosclerotic changes occurring in the internal organs. The tendency for this anæmia to disappear and to be replaced in the terminal state by a progressive increase in both elements, which in some cases passed the normal limits, does not, as far as recorded,[1] find its counterpart in other diseases, and is more difficult of explanation. The most rational explanation would be that it was due to a concentration of the blood, dependent upon a lack of ingestion of fluids and food during the terminal period. This did occur in the paretics during the latter part of the terminal period, and in some cases the abstinence was complete during the last few days.

In order to determine the importance of this factor several moribund cases suffering from inanition were studied. In six such cases in which the examination was made from four to twenty-seven hours ante-mortem, and in which there was an absence of the ingestion of food and water, as well as an absence of temperature or demonstrable inflammatory condition, the hæmoglobin was found to be low in all cases except one (93 per cent.). The erythrocytes in these cases were within normal limits except in this one case, in which they reached 6,155,000. Sluggish circulation was evident in the moribund cases as well as in the moribund paretics, by the slow flow of the blood and by the appearance of an extremely dark-colored drop at the point of puncture. Judging from these facts one feels safe in the assumption that the high percentage of hæmoglobin and the tendency to a polycythæmia of the terminal paretic state is not due to concentration of the blood dependent upon lack of ingestion of food and fluids or to the weakened heart's action and sluggish circulation. Furthermore, this condition of the paretic blood was in the majority of cases coincident with the onset of the terminal state and was in existence some days or weeks before the moribund state appeared.

The two pathological conditions observed in the leukocytes which merit comment are the appearance of a terminal leukocytosis coincident or nearly so with the terminal mental state and the presence of a leukocytosis accompanying paretic attacks of an epileptiform nature. In considering the terminal leukocytosis one must eliminate the presence of any inflammatory conditions which might give rise to it. In Case IX. bronchopneumonia appeared two days before death. The final count was taken ten hours later and showed a fall in the leukocytes from 13,700 to 10,700. With this exception there was no physical sign of any inflammatory process in the five cases not examined post-mortem, and no pathological evidence of it in the six cases in which an autopsy was performed.

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[1] Prof. Ewing informs me that he has observed a somewhat similar tendency in isolated cases of cancer and of tuberculosis.

This leukocytosis should not be confounded with the moribund leukocytosis mentioned by Cabot and other writers, as it appears some time before the moribund state. In accord with their statements it might be added that our six moribund cases, examined from four to twenty-seven hours ante-mortem, showed a leukocytosis varying from 13,000 to 17,000, being highest in the cases four and five hours ante-mortem. Moribund leukocytosis is believed to arise either from stasis or from terminal "intoxication." The former explanation cannot apply to prolonged terminal paretic leukocytosis, as the sluggish circulation and weakened heart action did not appear until just previous to death. The preponderance of experimental evidence goes to prove that leukocytosis should be regarded as a reaction to the presence of a chemical substance in the blood, the function of the leukocytosis being to remove these substances.

The only chronic non-febrile non-inflammatory disease process comparable with dementia paralytica in which a terminal leukocytosis has been observed is chronic nephritis, terminating in uræmia. In this disease Cabot found an absence of leukocytosis in the great majority of cases during the progress of the disease until the uræmic state when leukocytosis appeared in thirty-four of forty cases. This concurrence is most significant, not only in establishing the toxic origin of the terminal state and its leukocytosis, but also the toxic origin of the disease.

The presence of the leukocytosis accompanying paralytic attacks has already been established by Capps. Our limited observations on this matter simply bring additional evidence. In explanation of this phenomena, here again the only recourse is to the toxic theory. The only disease presenting symptoms comparable with the paralytic attacks of dementia paralytica is idiopathic epilepsy. The blood conditions in this disease have been studied by Kroubmiller and Pugh. Kroubmiller[1] studied twelve cases, and claims that at the time of the attack the total quantity of leukocytes is increased and that the increase diminished with every new attack. It is highest one hour after the attack. This increase is due to the relative and absolute increase in the lymphocytes with a relative decrease of the other cells. Pugh[2] studied twenty cases of idiopathic epilepsy. His observations were confined to a single examination from one to twenty-four hours after the occurrence of one or more convulsions in seventeen of the cases, and in three cases an examination also in the interparoxysmal period. He found that a leukocytosis occurred following seizures, which diminished with each convulsion following the first and was less marked in epileptic status.

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[1] Idem cit.

[2] Brain, Winter, 1902.

In this leukocytosis there was an increase in the small and large lymphocytes and a diminution of the polymorphonuclear variety.

These observations in epilepsy, which are in accord with the results of Capps and our own in dementia paralytica, add further weight to the toxic theory of the origin of this disease.

The question naturally arises, if this theory be true, Why are not the states of paretic excitement and stupor, which clinically seem to indicate an intensification of the toxic state, accompanied by a leukocytosis? It is a recognized clinical fact that the paralytic attacks are regularly followed by greater mental impairment. The same is true of the excited and stuporous states, at which times the disease usually makes greater inroads upon the mentality of the patient. Furthermore, a similar condition appears to exist in the terminal state whether the outward manifestations are those of excitement, stupor, or simple inanition. The only explanation for the absence of a leukocytosis in the paretic excitement and paretic stupor not terminal is that the toxic state is not intense enough to produce it.

A further pathological change which occurs in striking uniformity is the increase of the polymorphonuclear variety of leukocytes throughout the course of the disease, for which we can offer no explanation.

The results of this systematic examination of the paretic blood corresponds with those obtained by earlier investigators in reference to the progressive anæmia, but they controvert the observation of Smyth that there is a cessation of the progressive fall of hæmoglobin during periods of great exaltation. The recorded observations on the leukocytes have been : a diminution at the end (Macphail), a diminution in seven of fourteen cases (Jelliffe), a slight increase (Somers), a moderate leukocytosis, except near the onset (Capps), and leukocytosis with the exalted state (Jelliffe). Our study does not accord with any of these views, though examinations made irregularly during the course of the disease in any of our cases might easily have brought results in accord with all of them, except those of Capps in reference to the leukocytosis accompanying paralytic attacks. The observation of Jelliffe that a leukocytosis accompanies exalted conditions is improbable, as it occurred in only one of six exalted periods.

CONCLUSIONS. Dementia paralytica is accompanied by a moderate and progressive anæmia, involving, especially, the hæmoglobin and becoming more marked as the disease progresses.

The terminal state of the disease is accompanied by a rise in the hæmoglobin, erythrocytes, and a leukocytosis.

Paralytic attacks are accompanied by a leukocytosis.

Throughout the disease process there is a pathological increase of polymorphonuclear leukocytes which reaches its height during the terminal state.

States of paretic excitement, stupor or quiescence, not terminal, are not accompanied by any characteristic blood changes.

The presence of a leukocytosis accompanying the terminal state and paralytic attacks is significant evidence in favor of the toxic origin of the disease.

I desire to express my appreciation of the faithful work done by Messrs. Burr, Ward, and Stone in making the blood-counts, and particularly the assistance given by Mr. H. C. Stone in compiling the statistics of the counts and in arranging the histories of the cases.

The accompanying tables represent only the terminal stage of the disease, and in some cases a part of the period just preceding.

TABLE I.

Month of disease.	Hæmoglobin.	Erythrocytes.	Leukocytes.	Poly. leukocytes.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Weight.	Temperature.	Stages of the disease.
Case No. 1.										
25th mo. 4th	77	4,613,000	5,000	78.6	18.6	2.2	0.6	143	Normal	Moderate excitement.
25th " 11th	70	4,653,000	5,800	81.8	12.6	5.6	0	141	"	
25th " 18th	85	4,933,000	6,000	83.2	14.0	2.4	0.4	134	"	
25th " 25th	78	5,166,000	7,266	89.6	9.8	2.0	0.6	131	"	
26th " 2d	78	5,584,000	8,300	85.8	10.2	4.0	0	119	"	
26th " 9th	70	5,475,000	11,533	81.2	14.2	4.6	0	118	"	Terminal great excitement.
26th " 15th	82	5,631,000	9,100	92.0	5.8	2.0	0.2	100	[1]	
26th " 17th	80	5,688,000	23,900	96.0	2.8	1.2	0	...		
26th " 19th	93	5,457,000	22,900	95.6	3.0	1.4	0	...		
26th " 22d	92	6,386,000	13,500	92.8	6.0	1.2	0	85		

TABLE II.

Case No. 2.										
17th mo. 9th	72	4,568,000	8,400	85.2	12.2	2.2	0.4	102	Normal	Quiescent.
17th " 23d	80	5,786,000	5,600	83.4	11.4	3.6	1.6	97	"	
17th " 30th	89	5,306,000	10,533	80.8	14.2	4.4	0.6	97	"	
18th " 7th	70	5,671,000	8,400	80.0	13.2	6.0	0.8	94	"	
18th " 15th	62	5,453,000	8,200	79.6	14.0	4.2	2.0	94	"	
18th " 22d	83	5,182,000	9,100	77.6	16.8	4.6	1.0	92	"	
18th " 29th	67	4,888,000	8,400	90.0	6.6	3.4	0	88	"	Terminal stupor.
19th " 4th	82	5,982,000	16,100	86.4	9.8	3.2	0.6	79	"	

TABLE III.

Case No. 4.										
18th mo. 2d	65	4,515,000	7,000	78.8	16.0	5.0	0.2	[2]	Normal	Terminal stupor.
18th " 16th	68	4,916,000	10,160	81.6	15.2	2.4	0.8		"	
18th " 31st	70	4,222,000	8,700	86.2	9.4	4.4	0		"	
19th " 12th	70	4,697,000	14,660	94.2	3.8	2.0	0		"	

TABLE IV.

Case No. 5.										
16th mo. 5th	83	5,133,000	7,600	81.2	13.1	4.5	1.1	111	Normal	Excitement.
16th " 12th	83	5,442,000	7,600	82.2	10.4	6.0	1.4	110	"	"
16th " 19th	85	5,622,000	6,700	84.0	10.3	4.0	1.7	110	"	"
16th " 26th	85	5,724,000	11,400	84.8	10.0	4.4	0.8	109	"	"
17th " 2d	86	5,624,000	11,300	84.4	11.6	3.6	0.4	...	"	"
17th " 5th	76	5,162,000	17,200	93.2	3.6	3.2	...	...	"	Terminal stupor.
17th " 9th	86	6,333,000	14,267	93.4	4.0	1.4	1.2	85	"	

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[1] Could not be taken.

[2] Could not be taken.

TABLE V.

Month of disease.	Hæmoglobin.	Erythrocytes.	Leukocytes.	Poly. leucocytes.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Weight.	Temperature.	Stages of the disease.
Case No. 6.										
7th mo. 31st	85	5,488,901	6,300	82.2	12.8	4.6	0.4	[1]	Normal	Terminal stupor.
8th " 10th	70	4,573,000	6,500	86.2	7.8	5.4	0.6		99.4	
8th " 17th	68	4,769,000	10,000	85.0	9.4	4.4	1.2		98.6	
8th " 26th	60	3,711,000	17,720	93.0	2.6	4.4	0		......	
9th " 2d	65	4,484,000	25,000	83.0	14.0	2.2	0.8		96.4	

TABLE VI.

Case No. 7.										
19th mo 18th	70	4,516,000	6,600	70.6	21.2	6.2	2.0	113	Not taken	Excitement.
20th " 6th	85	5,293,000	5,533	66.0	24.4	6.8	2.8	107		"
20th " 20th	86	5,053,000	5,030	71.8	24.6	2.4	1.4	100		"
21st " 6th	76	4,244,000	6,300	53.8	37.2	8.2	0.8	111		"
21st " 22d	78	4,400,000	5,900	54.4	39.0	3.6	3.6	112		"
22d " 5th	105	5,089,000	9,060	71.8	20.2	4.2	0.8	104		Terminal stupor.

TABLE VII.

Case No. 8.										
11th mo. 29th	85	5,800,000	7,400	80.4	13.2	5.2	1.2	157	Normal	Quiescent.
12th " 5th	85	4,942,000	10,660	84.0	10.2	4.0	1.8	157	"	
12th " 12th	90	5,408,000	10,900	81.4	13.2	4.0	1.4	155	"	
12th " 19th	97	4,693,000	16,500	92.0	5.6	2.0	0.2	...	"	Terminal excitement.
12th " 26th	102	6,302,000	17,800	79.2	14.6	5.2	1.0	128	"	
12th " 27th	105	6,373,000	17,920	81.8	15.6	1.6	1.0	...	"	
13th " 2d	120	7,551,000	27,000	91.6	6.0	2.0	0	121	"	

TABLE VIII.

Case No. 9.										
29th mo. 29th	82	5,547,000	7,750	76.6	17.2	4.2	2.0	145	......	Terminal stupor.
30th " 5th	73	4,500,000	8,666	76.4	15.4	6.0	2.2	145	97.2	
30th " 12th	80	4,700,000	10,000	87.4	7.0	5.2	0.4	139	99.6	
30th " 18th	78	4,131,000	13,730	84·8	11.6	3.2	0.4	129	99.6	
30th " 22d	...	3,600,000	10,700	...	...	...	...	...	105.0	

TABLE IX.

Case No. 10.										
24th mo. 8th	65	4,538,000	5,100	76.4	20.4	2.6	0.6	161	Normal	Terminal stupor.
24th " 15th	78	4,889,000	7,000	65.0	28.2	5.6	0.6	...	"	
24th " 22d	80	5,333,000	8,200	80.4	12.8	5.2	1.6	...	"	
24th " 30th	90	6,271,000	15,860	86.2	6.8	6.8	0.2	107	"	

TABLE X.

Case No. 11.										
26th mo. 8th	80	5,533,000	7,860	74.2	22.4	3.2	0.2	144	Normal	Quiescent.
26th " 24th	68	4,862,000	6,000	76.0	19.6	4.2	0.2	137	"	"
27th " 5th	75	4,747,000	8,860	82.2	14.2	3.2	0.4	137	"	"
27th " 19th	80	5,328,800	7,260	81.4	14.8	3.6	0.2	134	"	"
28th " 2d	78	5,333,000	8,800	77.8	17.2	4.4	0.6	130	"	Stupor.

[1] Could not be taken.